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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/486,293	08/22/2000	JONATHAN A COOPER	14538A-004010US	3432

7590 12/29/2005

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EXAMINER	
GEBREYESUS, KAGNEW H	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 12/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/486,293	COOPER ET AL.	
	Examiner	Art Unit	
	Kagnew H. Gebreyesus	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 2 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09/19/05*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-8 and 10-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 5-8, 10-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants response on September 19, 2005 to the Office Action filed on March 15, 2005 is acknowledged. Claims 1-18 are currently pending. Claims 1, 5, 6, 10, 1 1, 13 and 18 have been amended. Claims 4, 9 and 19 through 35 are cancelled.

Withdrawn - Claim Objections

1. The claim objection under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim has been withdrawn following the amendment.

Withdrawn - Claim Rejections - 35 USC § 112

2. The rejection of claims 6-9 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention has been withdrawn following the amendment reciting the specific hybridization condition.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 1 and dependent claims 3, 2, 5, 10-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1 applicants recite:

"... mammalian Dabl (Disabled protein 1) as depicted in SEO ID NO: 3, or a fragment thereof, wherein the mammalian Disabled protein comprises a phosphotyrosine binding domain and can associate with the SH2 domain of Src, Abl or Fyn, or a complementary sequence thereof". Does

the fragment also comprise a phosphotyrosine binding domain and can it associate with the SH2 domain of Src, Abl or Fyn?

For examination purposes the examiner assumes that the fragments do not comprise a phosphotyrosine binding domain or associate with the SH2 domain of Src, Abl or Fyn.

Furthermore, claim 5 as amended is not further limiting as any nucleic acid within the scope of claim 1 will hybridize as recited in claim 5.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 11 and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims are rejected for the recitation " substantially depicted". The metes and bounds of the term substantially depicted is unclear. Clarification is required.

Withdrawn - Claim Rejections - 35 USC § 112

The claim rejection of claims 1-3, 5, 9, 10 and 13-17 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. This rejection has been withdrawn following the amendment limiting the claim to SEQ ID NO: 3.

Withdrawn - Claim Rejections - 35 USC § 102

7. The rejection of claims 1, 2, 5, 6, 7 and 9 under 35 U.S.C. 102(b) as being anticipated by Bonaldo et. al. is withdrawn for the following reason. This rejection was based on a reference by Bonaldo et al entitled Normalization and subtraction: two approaches to facilitate gene discovery in the journal Genome Research 6 (9), 791-806 (1996). However upon further evaluation, the nucleotide sequence with accession number BE949139 indicated in NCBI was not available to the public until October, 3rd, 2000. Therefore the rejection has been withdrawn.

Maintained - Claim Rejections - 35 USC § 102 and 103

Claims 1- 3, 5 are rejected under 35 U.S.C. 102(a) as being anticipated by Howell et. al. (Genbank accession Y08379).

Applicants argue:

"...Applicants note that the present application claims priority to US application serial number 60/056,473, filed August 21, 1997. The publication date of the GenBank submission is less than 12 months prior to the date of filing the priority application. Further, the GenBank submission was made by the two inventors of the present application. The submission also names a third co-author who is not a co-inventor of the claimed invention. As the date of disclosure is less than 12 months prior to the filing date of the priority application the GenBank submission is not a proper reference under 35 U.S.C. 102(a). The Examiner is respectfully requested to withdraw the present rejection..."

Applicants further advance the same reasoning for the rejection of claims 1- 3, 5-8, 10-18 (as they apply to previous claims 1-17) based on Howell et al., EMBO J. 16:121-132, 1997.

However Attorney's argument stating that a reference is applicant's own work is not sufficient given that other inventors/authors are included. To date applicants have not provided a declaration under 1.132 regarding inventorship therefore the rejections of claims 1- 3, 5 rejected under 35 U.S.C. 102(a) are maintained.

Likewise the rejection of claims 1-3, 5 and 6-8, 10-18 as applied to previous claims 6-18 rejected under 35 U.S.C. 103(a) as unpatentable over Howell et al are maintained. The explanation is given above and in the previous office action.

New Rejection:

Claim Rejections - 35 USC § 101

8. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-3, 5, 6-8, 10-18 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility. Claim 1 and dependent claims thereof are drawn to a polynucleotide encoding the polypeptide of SEQ ID NO: 3 and fragment thereof. The specification indicates identification of the mDab polypeptide based on its interaction with Src in a yeast two hybrid screen. Furthermore applicants disclose that the mDab1 mRNA is expressed as a variety of spliced mRNAs in the nervous system as in some cell lines and mDab1 proteins are differentially expressed and tyrosine phosphorylated during neuronal development. Applicants further assert that a complex is formed with cellular phosphotyrosyl proteins through a PTB binding domain. Finally applicants speculate that mDab appears to play a role as an adaptor protein that participates in development of the nervous system. Furthermore applicants disclose that the PTB of mDab1 interacts with a region of the amyloid precursor protein (APP) characteristic to Alzheimer's disease. Based on these findings applicants assert the utility of in the diagnosis and treatment of injury and disease conditions as diverse as metastatic cancer, reactive gliosis, neurodegenerative diseases and Alzheimer's Disease.

However these assertions are not specific and substantial as applicants have not substantiated the association of mdab1 binding or the association of it's PTB domain with the diseases mentioned above such that a skilled artisan would know how to use the claimed polynucleotides to diagnose or treat any of the recited diseases. Therefore, although applicants have taken an approach and direction that potentially may lead to elucidating the specific function of mDab1 gene and the fragments thereof, the claimed invention is incomplete and does not have a patentable utility until some actual and specific disease condition can be associated with the ability of mDab 1 (SEQ ID NO: 3) to bind to the SH2 domain of Abl, Fyn and or Src and/or it's PTB domain.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 5, 6-8, 11-12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification does not contain any disclosure of the structure of all DNA sequences of all mammalian mDab1 and fragments thereof. The genus of polynucleotides that encode polypeptides that comprise any mammalian Dab1 or any fragment thereof, is a large variable genus with the potentiality of encoding many different proteins from any mammalian source. Therefore, many structurally unrelated DNAs are encompassed within the scope of these

claims, including partial DNA sequences and sequences that have not been disclosed by the specification. The specification discloses only a few (three) species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus including any polynucleotide encoding any polypeptide with the sole limitation of having a phosphotyrosine binding domain and being capable of associating with Src, Abl or Fyn as there are other genes encoding polypeptides such as e.g. p62 or SLM-1 with these attributes but are unrelated to mDab1. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Claims 1, 2, 5-8, 11 and 12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a DNA sequence of SEQ ID NO: 3, does not reasonably provide enablement for any fragment thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1, 2, 5-8, 11 and 12 are so broad as to encompass any fragment of a polynucleotide that can or cannot encode a phosphotyrosine domain containing peptide from any mammalian species. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides encoding functionally unrelated polynucleotide sequences encoding polypeptides with or without phosphotyrosine binding domains containing polypeptides and may or may not be capable of associating with Src, Abl or Fyn as broadly encompassed by the claims. Since the polynucleotide sequence encoding

amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to SEQ ID NO: 3 or a fragment with a phosphotyrosine-binding domain AND can associate with the SH2 domain of Src, Abl or Fyn.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, or any fragment thereof as encompassed by the instant claims, and the positions within a polynucleotide encoding the polypeptide's sequence where nucleic acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any molecule and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass any polynucleotide that will hybridize to SEQ ID NO: 2, any ortholog, allelic or splice variant of the polypeptide of SEQ ID NO: 3 encoded by SEQ ID NO: 2, as well as any polynucleotide comprising 15-60 nucleotides that can hybridize to SEQ ID NO: 2 because the specification does **not** establish: (A) regions of the polynucleotide sequence which may be modified without necessarily affecting the protein structure necessary for it's ability to specifically associate with

Src, Abl or Fyn or conserve the PTB domain; (B) the general tolerance of the polynucleotide encoding the specific mDab1 to modification and extent of such tolerance; (C) a rational and predictable scheme for selecting a fragment of a polynucleotide sequence with an expectation of retaining the ability to hybridize to a polynucleotide sequence encoding mDab1 encoded by SEQ ID NO: 2 (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including mammalian Dab1 Disabled protein 1, or a fragment thereof or a probe comprising an oligonucleotide capable of specifically hybridizing to a polynucleotide sequence of SEQ ID NO: 2. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of any fragment or probes comprising an oligonucleotide capable of specifically hybridizing to a polynucleotide sequence of SEQ ID NO: 2 is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

2. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kagnew H. Gebreyesus whose telephone number is 571-272-2937. The examiner can normally be reached on 8:30am-5:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Achutamurthy ponnathapura can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Kagnew Gebreyesus PhD.

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